Case Report: Successfully Managed Acute Transverse Myelitis Related to Scrub Typhus and Serial Image Findings

Jae Sung Yun,† Ji Soo Song,‡ Eun Jung Choi,§ Jeong-Hwan Hwang,∥ Chang-Seop Lee,∥ and Eun Hae Park*†

†Seoul Regional Military Manpower Administration, Seoul, Korea; ‡Department of Radiology, Research Institute of Clinical Medicine of Chonbuk National University–Biomedical Research Institute of Chonbuk National University Hospital, Jeonju, Korea; ∥Department of Internal Medicine, Research Institute of Clinical Medicine of Chonbuk National University–Biomedical Research Institute of Chonbuk National University Hospital, Jeonju, Korea

Abstract. Central nervous system involvement manifesting as meningitis or meningoencephalitis is a known complication of scrub typhus, but very few spinal cord lesions such as acute transverse myelitis (ATM) have been reported in association with this disease. Scrub typhus patients with a spinal lesion present with neurologic symptoms including dysuria, motor, and sensory weakness. Herein, we describe a rare case of ATM associated with scrub typhus. Clinical characteristics, cerebrospinal fluid cytology, Orientia tsutsugamushi serum antibody titer, and serial magnetic resonance imaging scans resulted in a diagnosis of ATM associated with scrub typhus.

INTRODUCTION

Symptoms of scrub typhus are usually mild and the clinical course self-limited, with spontaneous recovery after a few days.1 However, some cases are more severe and protracted and may involve the lungs, heart, liver, spleen, kidney, gastrointestinal tract, and central nervous system (CNS).1,2 CNS involvement in scrub typhus can manifest as meningitis or meningoencephalitis.1,3 Other neurologic manifestations include cerebral infarction and brain hemorrhage.4–6 Although there are reports of brain lesions and meningitis in patients with scrub typhus, reports of spinal cord involvement, such as acute transverse myelitis (ATM) associated with scrub typhus, are extremely rare.7,8 ATM is a focal inflammatory disorder of the spinal cord, characterized clinically by acute or subacute motor, sensory, and autonomic dysfunction.9 Proceeding nonspecific fever, nausea, or muscle pain, possibly indicating viral infection, are common.10 ATM is associated with multiple sclerosis, systemic mixed connective tissue disorder, direct infection of the spinal cord (i.e., Mycoplasma or herpes simplex virus), and vascular causes (i.e., infarct or vascular malformation), but can also appear without an established etiology.11 There have been no previous reports with serial image findings or reports of resolution of ATM associated with scrub typhus. Herein, we report a successfully managed case of scrub typhus–associated ATM and the serial magnetic resonance imaging (MRI) findings.

CASE REPORT

A 67-year-old male patient was transferred to our institution with acute onset progressive and ascending lower extremity weakness and voiding difficulty for 3 days. He also had fever and chills. Twenty days prior, he had engaged in outdoor activities; 3 days later he developed flu-like symptoms including fever, chills, and general malaise. He underwent conservative treatment with over-the-counter medications, during which time he went hiking again. Eleven days after the original outdoor activity, his symptoms progressed and he visited a local clinic. On physical examination, a red crusted eschar was observed on the patient’s neck that had not noted previously. He was hospitalized without delay, and doxycycline was administered under suspicion of scrub typhus related to outdoor activities and appearance of eschar. However, his symptoms persisted, and after 9 days in hospital, acute urinary retention and progressive weakness of both lower legs developed.

At the time of admission to our hospital, he had fever, chills, myalgia, dysuria, and weakness in both legs. Physical examination revealed an obvious eschar on the neck (Figure 1), which still had a crust in place. On neurologic examination, motor power was decreased in both lower extremities (grade 2/5). Sensory testing showed hypesthesia to touch on the lateral side of the left lower extremities, including the buttock and inguinal area. Babinski reflexes were 2+ in both lower extremities. Urine (800 mL) was drained by Foley catheter. The results of routine hematologic testing were normal except for an elevated erythrocyte sedimentation rate (26 mm/hour) and alanine aminotransferase (59 IU/L). Cerebrospinal fluid (CSF) tests showed a white blood cell count of 18/mm³, an elevated concentration of protein (76.4 mg/dL), and a decreased concentration of glucose (43 mg/dL). Routine culture and Gram staining of CSF were negative. The results of blood culture were normal. The diagnosis of scrub typhus was validated by positive results on an indirect immunofluorescence assay (serum antibodies for Orientia tsutsugamushi; 1:2,560). Cryptococcal antigen test and serological tests for Hantavirus, Epstein–Barr virus, cytomegalovirus, Leptospira, Mycoplasma, and Legionella were all negative.

Brain MRI and whole-spine MRI (Figure 2A) were performed without delay under suspicion of encephalitis, Guillain–Barré syndrome (GBS), or myelitis, but they revealed nonspecific findings. However, 12-hour follow-up enhanced whole-spinal MRI scans demonstrated swelling of the spinal cord with high-signal intensity on T2-weighted images, with poor enhancement between the lower C-spine and T5. The lesion mainly involved the central gray matter (Figure 2B–E). A diagnosis of ATM was made, and steroid treatment was initiated.
Fever, chills, and myalgia disappeared completely after 2 days. On day 5, voiding difficulty improved, and motor power of both lower extremities increased to grade 3/3. On day 7, follow-up spinal MRI scans revealed a dramatically decreased extent of increased signal intensity of the spinal cord, with only subtle signal change remaining in the gray matter (Figure 3A). On day 10, after 7 days of steroid pulse therapy by injection, the steroid intake method was changed to oral administration. Motor power in both lower extremities improved to grade 4/4. On day 16, the patient was able to void voluntarily. On day 20, he was transferred to the rehabilitation department of our hospital, and on day 40, he was discharged with grade 4+/4+ motor power of his lower extremities. Neurological examination on outpatient follow-up at 3 months revealed near-complete resolution of motor power of the lower extremities (grade 4+/4+), and follow-up MRI showed complete resolution of increased signal intensity in the spinal cord (Figure 3B). Eschar was photographed again on the 28th day after initial symptoms (Figure 1B). The crust disappeared completely, leaving only a whitish scar-like macule (indicating fibrosis).

Dermatoscopy revealed a healed lesion with red-brown hyperpigmentation of the surrounding erythema (Figure 1C).

**DISCUSSION**

Scrub typhus can be diagnosed based on patient history and clinical features as well as serologic tests. An eschar at the wound site is the single most useful diagnostic clue. In our case, we were able to diagnose scrub typhus because of the presence of an eschar on the neck, a history of outdoor activity, and a significant increase in the *O. tsutsugamushi* serum antibody titer with typical clinical symptoms of fever and malaise.

CNS involvement in scrub typhus is not uncommon. CNS involvement due to *O. tsutsugamushi* infection can be caused by direct invasion of the CNS by this organism, as has been demonstrated by polymerase chain reaction (PCR) of CSF, or by microinfarcts in the brain due to the unique propensity of *O. tsutsugamushi* to infect vascular endothelial cells. Pai and others identified *O. tsutsugamushi* on CSF PCR analysis in 24% of patients with scrub typhus.
Autopsy studies have revealed involvement of the CNS in almost all affected patients.\textsuperscript{1,14,15} Relatively commonly reported conditions reflecting CNS involvement are encephalitis and meningoencephalitis.\textsuperscript{1,13–16} However, at the time of admission to our hospital, our patient had progressive and ascending neurologic symptoms including weakness of both lower legs, hypesthesia, and dysuria, suggesting myelitis more than encephalitis, and there was no abnormal finding on brain MRI suspicious of encephalitis.

In our case, initial spinal MRI scans revealed nonspecific findings for the spinal cord. It is generally accepted that MRI performed immediately in patients with ATM may be normal but will demonstrate signal change over time.\textsuperscript{10,17,18} Twelve-hour follow-up MRI demonstrated swelling of the spinal cord and definite high-signal intensity between the lower C-spine and upper T-spine. The gray matter of the spinal cord was predominantly involved, and this is in general accordance with a previous report of scrub typhus–associated spinal cord involvement.\textsuperscript{16} This may be because the metabolic demand of cell bodies in the spinal gray matter is very high, making the gray matter the site most sensitive to ischemia.\textsuperscript{19} In the majority of cases, whether acute myelopathy is inflammatory is not self-evident in both clinical symptoms and imaging.\textsuperscript{10,20} Therefore, when a patient with myelopathy is systemically ill with fever and meningismus, prompt investigation of the causative agent is needed for appropriate management.\textsuperscript{10,11} For this reason, awareness of the causative infectious agent is of paramount importance.

GBS is an illness characterized by areflexic ascending paralysis with minimal sensory involvement. GBS is usually preceded by infection or other immune stimulation that induces an aberrant autoimmune response targeting peripheral nerves and their spinal roots.\textsuperscript{21,22} GBS has been previously reported as a complication of scrub typhus.\textsuperscript{23} GBS is associated with image findings including thickening of the conus medullaris and cauda equine with strong enhancement on postenhanced MRI scans, which were not observed in our case.\textsuperscript{24}

Delays in appropriate treatment can be one possible reason for severe complications. Lee and others reported that delayed administration of antibiotics may be a risk factor for fatal complications.\textsuperscript{25} In their study, patients with fatal complications had a significantly longer interval between symptom onset and antibiotic initiation compared with those without fatal complications (7.4 versus 12.3 days, respectively). In the present case, because the patient did not visit the clinic promptly and did not notice the eschar, the interval from symptom onset to doxycycline administration was 9 days. However, meningitis or meningoencephalitis can occur even in cases with appropriate drug therapy at an early stage.\textsuperscript{26}

In conclusion, the outcome of this case indicates that, when neurologic symptoms including dysuria and lower leg weakness are present in a patient with scrub typhus, spinal cord involvement should be suspected, and an appropriate treatment plan should be implemented. Serial MRI may be helpful for accurate diagnosis, since cord involvement may not be depicted on initial MRI.

REFERENCES


FIGURE 3. One-week follow-up sagittal T2-weighted fat saturation magnetic resonance imaging (MRI) of the lower C-spine and upper T-spine (A) shows improved extent and degree of spinal cord signal change. Only subtle signal change is noted in the gray matter (arrow). The high-signal intensity focus at T3 is due to an artifact (arrow head). Three-month follow-up sagittal T2-weighted MRI of the lower C-spine and upper T-spine (B) reveals complete disappearance of abnormal hyperintensity.